IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

IN RE: ZOLOFT (SERTRALINE HYDROCHLORIDE) PRODUCTS LIABILITY LITIGATION	:	**MDL NO. 2342**
	:	**12-MD-2342**
	:	
	:	**HON. CYNTHIA M. RUFE**
THIS DOCUMENT RELATES TO:	:	
ALL ACTIONS	:	

OPINION

Rufe, J. **April 5, 2016**

By Order filed April 17, 2012, the United States Judicial Panel on MultiDistrict Litigation transferred to this Court, for coordinated or consolidated pretrial proceedings, cases alleging that Zoloft (sertraline hydrochloride), "a prescription medication approved for the treatment of depression and other ailments, causes birth defects in children when their mothers ingest the drug while pregnant."[1] In rejecting arguments opposing centralization of the cases, the Panel determined that "while the specific birth defects alleged vary somewhat among the plaintiffs, all actions will share discovery relating to general medical causation; factual discovery will overlap concerning Pfizer's research, testing, and warnings; and expert discovery and *Daubert* motions will overlap to some degree."[2] These events common to the litigation having occurred, the Court now is presented with Defendants' motion for summary judgment in all pending cases.[3] Plaintiffs, through the Plaintiffs Steering Committee ("PSC"), oppose the

[1] Doc. No. 1 at 1.

[2] Doc. No. 1 at 2. *Daubert* motions are the method in federal court by which the admissibility of expert witnesses is determined. *See Daubert v. Merrill Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993).

[3] Doc. No. 1521; Reply at Doc. Nos. 1561, 1563. The motion was filed by Pfizer, Inc., its former division J.B. Roerig & Company, Pfizer International LLC, and Greenstone LLC. These Defendants may be referred to collectively as "Pfizer." The motion has been joined by Defendants Wolters Kluwer Health, Inc. and Wolters

motion.[4] The motion puts the following two questions before the Court: First, have Plaintiffs produced sufficient admissible evidence from which a reasonable factfinder could determine, by a preponderance of the evidence, that Zoloft caused Plaintiffs' injuries? Second, if they have not, what next?

I. BACKGROUND

Early in the MDL, the parties agreed to a schedule to govern proceedings in the MDL.[5] The schedule included discovery from Pfizer, the exchange of expert reports regarding general causation and hearings as to the admissibility of the expert testimony pursuant to *Daubert v. Merrell Dow Pharmaceuticals*.[6] At the initial hearings, the PSC offered the testimony of four expert witnesses[7] on the issue of general causation in an effort to establish that Zoloft, when used at therapeutic dose levels during human pregnancy, is a teratogen capable of causing a range of birth defects.[8] Plaintiffs primarily relied upon Dr. Anick Bérard, an epidemiologist.[9] By opinion dated June 27, 2014, the Court found that Dr. Bérard had failed to base her opinion upon

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Kluwer United States Inc., which published patient education information and are named in a relatively small number of cases. Doc. Nos. 1525, 1562.

[4] The only opposition was filed by the PSC [Doc. Nos. 1544-49]. The Court expressly granted all Plaintiffs' counsel the opportunity to submit any non-duplicative arguments in opposition to the motion within two weeks after receipt of the PSC's motion. *See* Pretrial Order No. 95 [Doc. No. 1529]. No additional briefs were filed.

[5] *See* Joint Motion [Doc. No. 285]; Pretrial Order No. 15 [Doc. No. 287, entered November 16, 2012].

[6] 509 U.S. 579, 593-94 (1993). Although, as Plaintiffs note, Pfizer proposed the early determination of the general causation issues, the schedule was agreed upon and included comprehensive discovery from Pfizer on numerous issues. Plaintiffs did not argue that they were unprepared for the *Daubert* proceedings, and assured the Court early on that they were "not scared of *Daubert*." Tr. Status Conf. 10/17/12 at 81 [Doc. No. 280] (Statement of Joseph J. Zonies, Esq.).

[7] The PSC initially put forward additional expert witnesses but withdrew them before the hearings.

[8] A teratogen is "[a]n agent that produces abnormalities in the embryo or fetus by disturbing maternal health or by acting directly on the fetus in utero." *Reference Manual of Scientific Evidence (Third)* at 628.

[9] "Epidemiology is the field of public health and medicine that studies the incidence, distribution, and etiology of disease in human populations." *Id.* at 551.

scientifically valid methodology and reasoning such that it could not be considered by a jury.[10] The Court determined that "Dr. Bérard's methodology involved a rejection of the importance of replicated statistically significant epidemiological findings demonstrating an association between Zoloft and a pattern of birth defects, substituting a novel technique of drawing conclusions by examining 'trends' (often statistically non-significant) across selected studies."[11] The Court also held that Dr. Bérard failed to address adequately those epidemiological studies that did not support her opinion.[12]

By opinion and order dated August 12, 2014, the Court excluded in part the opinions of the PSC's three other general causation witnesses, Dr. Robert Cabrera (a teratologist), Dr. Michael Levin (a molecular developmental biologist), and Dr. Thomas Sadler (an embryologist). The Court concluded that these experts could not testify that Zoloft caused birth defects in humans but could testify as to the limited question of the existence of plausible biological mechanisms by which altered concentrations of serotonin in a developing embryo could cause birth defects.[13] The Court held that "when epidemiological studies are equivocal or inconsistent with a causation opinion, experts asserting causation opinions must thoroughly analyze the strengths and weaknesses of the epidemiological research and explain why that body of research does not contradict or undermine their opinion."[14] These experts did not address the

[10] *In re Zoloft (Sertraline Hydrochloride) Prods. Liab. Litig.*, 26 F. Supp. 3d 449 (E.D. Pa. 2014).

[11] *Id.* at 465.

[12] *Id.* at 462.

[13] *In re Zoloft (Sertraline Hydrochloride) Prods. Liab. Litig.*, 26 F. Supp. 3d 466, 473 (E.D. Pa. 2014).

[14] *Id.* at 475.

epidemiological evidence, and because Dr. Bérard's report and testimony had been excluded they could not rely on her conclusions or testify as to human causation.[15]

The PSC filed a motion for partial reconsideration of the opinion excluding Dr. Bérard only. The Court denied this motion by opinion and order dated January 23, 2015, rejecting the argument that the Court erred by requiring replicated, statistically significant epidemiological findings to establish general causation.[16] The Court explained that:

> medical experts, and especially physicians opining as to specific rather than general causation, may rely on data other than statistical evidence from epidemiological studies, such as a differential diagnosis, which is a "technique generally accepted in the medical community." *In re Diet Drugs (Phentermine/Fenfluramine/Dexfenfluramine) Products Liab. Litig.*, 890 F. Supp. 2d 552, 561 (E.D. Pa. 2012) (citing *Heller v. Shaw Industries, Inc.*, 167 F.3d 146, 155 (3d Cir. 1999)). However, Dr. Bérard is an epidemiologist, not a physician, and the Court has evaluated the reliability of her methods accordingly. Moreover, the Court notes that, unlike the association at issue in *In re Diet Drugs*, which had not been the subject of any epidemiological study, the use of Zoloft during pregnancy has been the subject of many large epidemiological studies designed with the goal of identifying any associations between maternal SSRI /Zoloft use and a broad range of birth defects. Even so, the Court has evaluated Dr. Bérard's methods according to the *Daubert* principles, and did not apply any bright-line exclusionary rules to her causation analysis.[17]

While seeking partial reconsideration, the PSC also filed a motion for leave to introduce Nicholas Jewell, Ph.D., a biostatistics professor, as an additional expert witness on general causation with regard to cardiac defects.[18] The PSC argued in support of its motion that "Dr. Jewell's testimony is critically important to the plaintiffs in this litigation. Proof of general causation – that exposure to Zoloft was capable of causing plaintiffs' injuries – is a prerequisite

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[15] *Id.* at 476 n.45.

[16] *In re Zoloft (Sertraline Hydrochloride) Prods. Liab. Litig.*, No. 12-md-2342, 2015 WL 314159, at * 2 (E.D. Pa. Jan. 23, 2015).

[17] *Id.* at *2 n.6. It is important to note that in the *Diet Drugs* case, the parties did not dispute that the drugs could cause the disease at issue; instead, the parties disputed the latency period between a plaintiff taking the drugs and developing the disease. *In re Diet Drugs*, 890 F. Supp. 2d at 561-62.

[18] Dr. Jewell was the only additional expert the PSC sought leave to introduce.

to recovery by every plaintiff herein."[19] By opinion and order dated January 7, 2015, the Court granted the motion after balancing the interests of all parties to the MDL and weighing heavily "the indisputable fact that the evidence is of critical importance to Plaintiffs."[20] After these rulings, many cases alleging non-cardiac injuries were dismissed without prejudice by stipulation of the parties.[21]

Defendants raised a *Daubert* challenge as to the admissibility of Dr. Jewell's testimony and report.[22] After this motion was filed, the parties stipulated to the dismissal without prejudice of additional cases, including some alleging both cardiac and non-cardiac defects.[23] Defendants also filed a motion to strike new expert reports by Dr. Levin and Dr. Sadler, arguing that Plaintiffs were improperly attempting to re-litigate the admissibility of these experts' reports and testimony.[24] These reports purported to be case-specific to the two trial-ready cases,[25] although Dr. Levin did not address any opinions specific to these Plaintiffs, and Dr. Sadler essentially applied his earlier opinions to the individual Plaintiffs. By stipulation of counsel approved by the Court, Plaintiffs agreed to withdraw the reports and reserved "the right to file supplemental reports from Dr. Levin and/or Dr. Sadler at a later date to address any new evidence relevant to

[19] Doc. No. 1054-1 at 13. These statements likely constitute judicial admissions. *See Berckeley Inv. Group, Ltd. v. Colkitt*, 455 F.3d 195, 211 n.20 (3d Cir. 2006) ("Judicial admissions are concessions in pleadings or briefs that bind the party who makes them.").

[20] *In re Zoloft (Sertraline Hydrochloride) Prods. Liab. Litig.*, No. 12-md-2342, 2015 WL 115486, at * 2 (E.D. Pa. Jan. 7, 2015).

[21] The Court had granted all Plaintiffs asserting non-cardiac injuries an opportunity to submit their own expert reports as to general causation. Pretrial Order No. 83 [Doc. No. 1165].

[22] Doc. No. 1210. At the same time, the PSC filed a motion to exclude the testimony of defense expert Dr. Robert Gibbons, *see* Doc. No. 1212; that motion was later dismissed as moot. Doc. No. 1498.

[23] *See* Pretrial Order No. 97 [Doc. No. 1565].

[24] Doc. No. 1372.

[25] The trial-ready cases, which were the cases in which full discovery regarding the Plaintiffs was conducted, are *Long v. Pfizer*, Civil Action No. 12-2595, and *Goulet v. Pfizer*, Civil Action No. 12-2441.

their opinions which may come to light, and the right to offer their testimony" in the cases set for initial trials.[26] Defendants reserved "all of their rights to file objections or motions challenging any report and/or opinion of" these experts.[27]

By opinion and order dated December 2, 2015, the Court excluded Dr. Jewell's report and testimony pursuant to Federal Rules of Evidence 403 and 702.[28] The Court concluded after hearing testimony over several days that Dr. Jewell failed to consistently apply the scientific methods he articulated, deviated from or downplayed certain well-established principles of his field, and inconsistently applied methods and standards to the data so as to support his *a priori* opinion.[29] Significantly, the Court found that Dr. Jewell failed to address adequately all of the available epidemiological studies, particularly more recent studies that did not replicate the results in earlier studies, even though these studies included and expanded upon the populations in the earlier studies.[30] The Court also concluded that Dr. Jewell improperly attempted to rely upon internal Pfizer documents because such partial literature reviews are not the kinds of information generally relied upon by statisticians, and because to the extent that the documents expressed Pfizer's preliminary concerns about product safety, warranting further investigation, and were not final conclusions drawn by Pfizer (as Pfizer argued), Dr. Jewell's use of them would potentially be misleading to a jury.[31] Pfizer moved for summary judgment immediately after this ruling.

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[26] Doc. No. 1452.

[27] *Id.*

[28] *In re Zoloft (Sertraline Hydrochloride) Prods. Liab. Litig.*, No. 12-md-2342, 2015 WL 7776911 (E.D. Pa. Dec. 2, 2015).

[29] *Id.* at *16.

[30] *Id.* at *7.

[31] *Id.* at *12.

II. LEGAL STANDARDS

A court will award summary judgment on a claim or part of a claim where there is "no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law."[32] A fact is "material" if resolving the dispute over the fact "might affect the outcome of the suit under the governing [substantive] law."[33] A dispute is "genuine" if "the evidence is such that a reasonable jury could return a verdict for the nonmoving party."[34]

In evaluating a summary judgment motion, a court "must view the facts in the light most favorable to the non-moving party," and make every reasonable inference in that party's favor.[35] Further, a court may not weigh the evidence or make credibility determinations.[36] Nevertheless, the party opposing summary judgment must support each essential element of the opposition with concrete evidence in the record.[37] "If the evidence is merely colorable, or is not significantly probative, summary judgment may be granted."[38] This requirement upholds the "underlying purpose of summary judgment [which] is to avoid a pointless trial in cases where it is unnecessary and would only cause delay and expense."[39] Therefore, if, after making all reasonable inferences in favor of the non-moving party, the court determines that there is no genuine dispute as to any material fact, summary judgment is appropriate.[40]

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[32] Fed. R. Civ. P. 56(a).

[33] *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 248 (1986).

[34] *Id.*

[35] *Hugh v. Butler County Family YMCA*, 418 F.3d 265, 267 (3d Cir. 2005).

[36] *Boyle v. County of Allegheny*, 139 F.3d 386, 393 (3d Cir. 1998).

[37] *Celotex Corp. v. Catrett*, 477 U.S. 317, 322-23 (1986).

[38] *Anderson*, 477 U.S. at 249-50 (internal citations omitted).

[39] *Walden v. Saint Gobain Corp.*, 323 F. Supp. 2d 637, 641 (E.D. Pa. 2004) (citing *Goodman v. Mead Johnson & Co.*, 534 F.2d 566, 573 (3d Cir. 1976)).

[40] *Wisniewski v. Johns–Manville Cor*p., 812 F.2d 81, 83 (3d Cir. 1987).

In ruling on the summary judgment motion, the Court has determined that it is not required to apply the law of any particular jurisdiction. Although Plaintiffs argue at various points in their opposition that the Court should apply the state or federal law applicable to the states where the trial-ready Plaintiffs live, Plaintiffs have not cited cases from any jurisdiction holding that the complex scientific question of whether a prescription drug is a teratogen can be answered without expert testimony or based on circumstantial evidence, and the legal principles upon which the Court has relied tend to be consistent across jurisdictions.[41]

III. DISCUSSION

Defendants argue that having failed to produce an expert who can establish general causation, Plaintiffs cannot prevail on any of their claims. Plaintiffs argue that there is substantial evidence of causation, including reports of adverse events, internal Pfizer documents that Plaintiffs say admit to a positive association between maternal use of Zoloft and cardiac defects, the evidence of biological plausibility from Dr. Levin and Dr. Sadler, differential diagnoses performed by a pediatric cardiologist that can establish both general and specific causation on a case-by-case basis, and an expert opinion by the former commissioner of the Food and Drug Administration ("FDA"). Although the Court has considered Plaintiffs' evidence in full, the Court will not engage in an *ad hoc* third round of *Daubert* proceedings, as to do so would provide Plaintiffs "with an open-ended and never-ending opportunity to meet a *Daubert*

[41] *See* W. Ertmer, *Just What the Doctor Ordered: The Admissibility of Differential Diagnosis in Pharmaceutical Product Litigation*, 56 Vand. L. Rev. 1227, 1258 (2003) (Although "state law varies considerably with respect to the quantum of evidence required to support a finding of causation . . . the general rule across jurisdictions is that satisfaction of the causation element requires evidence of both general and specific causation." (footnotes omitted)). *Cf. In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717, 751 (3d Cir. 1994) ("If the [state-court] rule conflicts with federal rules and is rationally capable of classification as procedural rather than substantive, then, as a federal court, the district court ignores the rule and applies federal rules instead. But the determination of whether a particular evidentiary ruling involves federal procedural law or state substantive law, can be difficult. Often admissibility issues overlap with substantive concerns such as standards of proof." (internal quotation marks and citations omitted)).

challenge until [they] 'get[] it right.'"[42] Plaintiffs essentially attempt to proceed as if general causation has not already been litigated extensively, as if the motion for leave to present Dr. Jewell was superfluous, and as if the withdrawal of the supplemental reports of Dr. Sadler and Dr. Levin was of no effect. The Court rules within the full context of the MDL proceedings, mindful of all prior rulings and procedural orders.

A. Can Plaintiffs Establish General Causation?

"Causation has two levels, general and specific, and a plaintiff must prove both. General causation is whether a substance is capable of causing a particular injury or condition in the general population, while specific causation is whether a substance caused a particular individual's injury. Sequence matters: a plaintiff must establish general causation before moving to specific causation. Without the predicate proof of general causation, the tort claim fails."[43]

Plaintiffs proffered four experts on general causation in the first round of *Daubert* proceedings: Dr. Bérard, Dr. Cabrera, Dr. Levin, and Dr. Sadler. The Court concluded that not one of these experts could testify that Zoloft is capable of causing birth defects in humans. In the second round of *Daubert* proceedings, Plaintiffs with leave of Court proffered Dr. Jewell and without leave of Court submitted supplemental reports by Dr. Levin and Dr. Sadler. Plaintiffs withdrew the supplemental reports and the Court held after an extensive hearing that Dr. Jewell could not testify that Zoloft causes birth defects in humans. The Court must determine whether Plaintiffs are able to establish general causation without the excluded expert testimony.

In opposing Pfizer's motion, Plaintiffs have presented the Court with a prodigious record. The Court has reviewed the 405 asserted statements of material facts (to which Pfizer has

[42] *In re TMI Litig.*, 199 F.3d 158, 159 (3d Cir 2000), *amending*, 193 F.3d 613 (3d Cir. 2000).

[43] *Wells v. SmithKline Beecham Corp.*, 601 F.3d 375, 277-78 (5th Cir. 2010) (internal quotations and citations omitted).

responded) and the nearly 200 exhibits contained in six banker's boxes produced by Plaintiffs. The quantity of the evidence is not, however, coterminous with the quality of evidence with regard to the issues now before the Court. Aside from issues such as the submission of duplicative exhibits[44] and untranslated foreign-language documents,[45] statements and documents relating to the development, marketing costs, and profitability of Zoloft[46] are irrelevant to the question of whether Zoloft can cause birth defects. Plaintiffs have also submitted again the epidemiological studies that, pursuant to the Court's rulings with regard to Dr. Bérard and Dr. Jewell, fail to support claims of causation.[47] In addition, the PSC recently filed a supplemental submission that purports to be an "important epidemiology recent study," but which appears to be a statement by statisticians as to p-values and statistical significance that has been accepted for publication but not yet published.[48] This document, whatever its provenance, is not relevant to the issues on summary judgment; the Court will not belatedly revisit the *Daubert* rulings.

1. The Role of Epidemiological Evidence

Plaintiffs argue that epidemiological evidence is not required to establish general causation.[49] Although the legal concept is more nuanced than Plaintiffs present, nevertheless,

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[44] *See, e.g.*, Robinson Decl. Exs. 112, 117, 127, and 129. The Court also notes that the description of the documents in the declaration does not always match the documents as tabbed.

[45] *See* Robinson Decl. Ex. 93 (a document from Honduras in Spanish).

[46] *See* PSC's Statement of Controverted and Disputed Facts in Opposition to the Pfizer Defendants' Motion for Summary Judgment at ¶¶ 4-7.

[47] Robinson Decl. Exs. 153-63. The copy of the Louik (2007) study appears to be the original, inaccurate study, not the version corrected by the study authors as required by the *New England Journal of Medicine* in 2015. Robinson Decl. Ex. 153.

[48] Doc. No. 1569.

[49] *See Rider v. Sandoz Pharms. Corp.*, 295 F.3d 1194, 1198 (11th Cir. 2002) ("It is well-settled that while epidemiological studies may be powerful evidence of causation, the lack thereof is not fatal to a plaintiff's case."). *See also Glasteller v. Novartis Pharms. Corp.*, 252 F.3d 986, 992 (8th Cir. 2001) (holding that the absence of epidemiological evidence does not doom a plaintiff's case, but its absence limited the available tools with which the plaintiff may prove causation). *But see Wade-Greaux v. Whitehall Labs., Inc.*, 874 F. Supp. 1441, 1453 (D.V.I.

this Court has not held to the contrary. Instead, the Court's rulings have followed the accepted principles that "epidemiology is the best evidence of general causation in a toxic tort case" and that "where epidemiology is available, it cannot be ignored."[50] As this Court held in the opinions on the biological experts:

> Several courts have held that positive human epidemiological studies are required to reach reliable conclusions as to whether an agent is teratogenic in humans, and causation opinions based primarily upon *in vitro* and live animal studies are unreliable and do not meet the *Daubert* standard. The Court agrees that reliable expert opinions about human causation generally should be supported by positive and replicated epidemiological studies, but reaches a narrower holding here. Specifically, the Court holds that when epidemiological studies are equivocal or inconsistent with a causation opinion, experts asserting causation opinions must thoroughly analyze the strengths and weaknesses of the epidemiological research and explain why that body of research does not contradict or undermine their opinion.[51]
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> . . .
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> Zoloft has been on the market and used during pregnancy for approximately twenty years, and a great deal of epidemiological research has been conducted and published. Therefore, the Court holds that any litigation experts on human causation in this MDL must address the epidemiological research. Where that body of research does not support the conclusions drawn by the experts, the experts must endeavor to reconcile the inconsistent epidemiological data with their opinions.[52]

In other words, in order to successfully opine on general causation (*i.e.*, that Zoloft can cause birth defects), any expert must account for the findings reached in the full universe of epidemiological studies.[53] In arguing against this determination, Plaintiffs rely on a case that

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1994), *aff'd* 46 F.3d 1120 (3d Cir. 1994) ("Absent consistent, repeated human epidemiological studies showing a statistically significant increased risk of particular birth defects associated with exposure to a specific agent, the community of teratologists does not conclude that the agent is a human teratogen.").

[50] *Norris v. Baxter Healthcare Corp.*, 397 F.3d 878, 882 (10th Cir. 2005) (citing cases).

[51] *In re Zoloft*, 26 F. Supp. 2d at 475 (footnotes omitted).

[52] *Id.* at 476.

[53] *Richardson v. Richardson-Merrell, Inc.*, 857 F. 2d 823, 830 (1988) ("These three types of studies then --- chemical, *in vitro*, and *in vivo*, cannot furnish a sufficient foundation for a conclusion that Bendectin caused the birth

arose in a different context, one in which epidemiological studies had not been published. The plaintiff in *Heller v. Shaw Industries, Inc.*,[54] sought recompense for respiratory illnesses allegedly caused by volatile organic compounds that emanated from carpeting manufactured by the defendant and installed in the plaintiff's home.[55] The Third Circuit rejected the notion that "a medical expert must always cite published studies on general causation" because to do so "would doom from the outset all cases in which the state of research on the . . . alleged causal agent was in its early stages," and would unacceptably impose a bright-line standard.[56] The decision in *Heller* does not stand for the proposition that existing epidemiological studies are irrelevant or need not be addressed and reconciled with an expert's opinions on causation. Plaintiffs cannot prevail by ignoring the epidemiological evidence.

2. Expert Evidence

a. Dr. Sadler and Dr. Levin

In opposing summary judgment, and in addition to the reports previously litigated in the *Daubert* proceedings, Plaintiffs have submitted reports that were the subject of the earlier motion to strike and were withdrawn pursuant to stipulation and order, and additional declarations dated 2016, relating to the *Long* and *Goulet* cases.[57] Pfizer has filed a motion to strike, arguing that

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defects at issue in this case. Studies of this kind, singly or in combination, are not capable or proving causation in human beings in the face of the overwhelming body of contradictory epidemiological evidence.").

[54] 167 F.3d 146 (1999).

[55] *Id.* at 149.

[56] *Id.* at 155. *Accord Milward v. Acuity Specialty Prods. Group, Inc.*, 639 F.3d 11, 24 (1st Cir. 2011) (distinguishing a case in which there was a lack of statistically significant epidemiological evidence from cases in the available epidemiological studies found no causal link).

[57] Robinson Decl. Ex. 164 (Dr. Levin's report of June 15, 2015); Fox Decl. Ex. 2 (Dr. Sadler's report in *Goulet* dated June 15, 2015); Smith Decl. Ex. 4 (Dr. Sadler's report in *Long* dated June 15, 2015); Plffs.' Ex. 8 (Dr. Sadler's declaration in *Goulet* dated Jan. 12, 2016); Plff.s' Ex. 10 (Dr. Sadler's declaration in Goulet dated January 21, 2016).

these submissions violate the Court's order approving the stipulation to withdraw the reports.[58] Pfizer also argues that the expert submissions address no new evidence and simply restate opinions excluded by the Court's second *Daubert* ruling. Plaintiffs argue that Pfizer was on notice that the experts would submit declarations specific to the *Long* and *Goulet* cases in opposition to summary judgment, and that a *Daubert* challenge could have been raised then, and that the submissions do not contravene the parties' Court-approved stipulation.

Plaintiffs cannot bring in new opinions by these experts or resurrect those previously excluded. The Court has ruled that neither Dr. Levin nor Dr. Sadler can testify that Zoloft, used in conventional doses, can cause birth defects in humans. As this opinion is inadmissible as to people in general, it must be inadmissible as to any particular Plaintiff.

The opinions that the Court previously held admissible remain admissible, and to the extent that Dr. Levin and Dr. Sadler have elaborated upon the bases for the admissible opinions, they are not barred from supplementing, but the Court will not allow its ruling to be circumvented under the guise of addressing specific causation or discussing new evidence. Nor will the Court sanction Plaintiffs' tactics in submitting reports, then withdrawing them without prejudice when challenged, only to bring them forth in opposing summary judgment. There was an appropriate time to offer these reports which may have withstood contest, but it is too late now.

The Court's *Daubert* ruling remains in effect: these experts cannot testify as to the ultimate issue of human causation. And because animal studies cannot overcome the contrary results of human epidemiological studies, the opinions do not support general causation, even in combination with the differential diagnoses by Dr. Abdulla.

[58] Doc. No. 1558.

b. Dr. Abdulla

Plaintiffs argue that differential diagnoses performed by Ra-Id Abdulla, M.D., with regard to the trial-ready *Long* and *Goulet* cases provide substantial evidence of general causation.[59] Dr. Abdulla, a pediatric cardiologist, is not a treating physician of either of the minor Plaintiffs, and was never designated as an expert on general causation. Therefore, it is procedurally improper, pursuant to the Court's pretrial scheduling orders, for Plaintiffs to tender him now, even as an expert on general causation as to individual Plaintiffs, and his opinions cannot be used to support general causation. Substantively, Dr. Abdulla's reports are also problematic.[60]

A differential diagnosis assumes that general causation has been established.[61] Although "there may be a case where a rigorous differential etiology is sufficient to help prove, if not prove altogether both general and specific causation,"[62] these are not such cases. "To properly perform a differential diagnosis, an expert must perform two steps: (1) 'Rule in' all possible causes of [the injury] and (2) 'Rule out' causes through a process of elimination whereby the last remaining potential cause is deemed the most likely cause" of the injury.[63] The expert must use scientifically valid methodology to rule in and rule out the potential causes.[64] However, reliable

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[59] Smith Decl. Ex. 1; Fox Decl. Ex. 3.

[60] *Cf.* Fed. R. Civ. P. 16(b)(4) ("A schedule may be modified only for good cause and with the judge's consent.").

[61] *Norris*, 397 F.3d at 885 (quotation marks and citation omitted).

[62] *C.W. v. Textron, Inc.*, 807 F.3d 827 (7th Cir. 2015) (emphasis omitted) (citing *Ruggiero v. Warner-Lambert Co.*, 424 F.3d 249, 254 (2d Cir. 2005)).

[63] *Feit v. Great West Life and Annuity Ins. Co.*, 271 F. App'x 246, 254 (3d Cir. 2008).

[64] *Ruggiero v. Warner-Lambert Co.*, 424 F.3d 249, 254 (2d Cir. 2005). A physician performing a differential diagnosis need not "rule out all alternative possible causes." *Heller*, 167 F.3d at 156 (internal quotation marks omitted).

methods for making a differential diagnosis "cannot sanitize an otherwise untrustworthy conclusion," and "good grounds" must exist for the physician to reach his conclusion.[65]

In his declarations dated January 28, 2016, Dr. Abdulla addresses "ruling in" potential causes of cardiac birth defects in the briefest possible fashion, simply stating that he "analyzed the relevant, publicly available scientific literature on the causes and risk factors for congenital heart disease including the review of experimental and human data related to serotonin (5HT) and selective serotonin reuptake inhibitors (SSRIs), including Zoloft, and abnormal cardiac development."[66] This bald statement does not constitute a scientific analysis for purposes of ruling in Zoloft as a cause of congenital heart disease. In his June 15, 2015 opinions, Dr. Abdulla opines that:

> As stated above, while there are studies which report a positive association which is not statistically significant but with a 95% Confidence Interval show an odds ratio reflecting increased risk and others which do not report a positive association, these [*sic*] are a variety of reasons these studies did not find statistical significance or increased risk, including lack of power for specific exposure-outcome analysis and/or the rarity of the defect to detect associations, which in my opinion does not refute the statistically significant and clinically important increase in risk for cardiac malformations demonstrated in the above peer-reviewed journals. Thus, considering the available evidence, it is my opinion that there is sufficient scientific evidence that Zoloft (sertraline) can cause a clinically important increase in the risk of congenital cardiac defects in infants exposed during the first trimester of gestation.[67]

Dr. Abdulla states reasons why a particular study may not have found a positive association, but this falls far short of establishing causation. Dr. Abdulla adds nothing new to the discussion of the epidemiological studies that neither Dr. Bérard nor Dr. Jewell could reliably interpret to establish general causation. Dr. Abdulla does discuss the difference between what is

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[65] *Heller*, 167 F.3d at 156.

[66] Pls.' Exs. 7& 9 at ¶ 15. Dr. Abdulla also stated that he considered "epidemiological evidence" and "all relevant scientific and medical literature." Pls.' Ex. 7 at ¶ 18.

[67] Smith Decl. Ex. 1 at 14; Fox Decl. Ex. 3 at 14.

clinically important (or significant) and what is statistically significant,[68] but clinical significance goes to the decisions made by the individual doctor and patient; it does not bear on general causation. Dr. Abdulla's specific causation opinion essentially assumes that general causation has been established; otherwise statements declaring, for example, that septal ventricular defects "have been encountered at a higher frequency in children exposed to SSRIs in-utero,"[69] put the rabbit in the hat, requiring the Court to simply take Dr. Abdulla's word for it.[70] Dr. Abdulla's reports do not provide "independently reliable evidence that that the allegedly dangerous drug or substance had harmful effects."[71]

It is important to note in this regard that birth defects "can be caused by a variety of factors, including genetic and chromosomal abnormalities and environmental agents."[72] Indeed, the etiology of many birth defects is currently unknown.[73] Congenital heart defects are the most common type of birth defects, occurring in as many as 1% of live births and affecting 40,000 infants in the United States each year.[74] Dr. Abdulla stated that he ruled out "maternal diabetes, family history of genetic or congenital heart diseases, arrhythmia, or sudden cardiac death, exposure to other medications (except prenatal vitamins)," environmental exposures, and

[68] Smith Decl. Ex. 1 at 11; Fox Decl. Ex. 3 at 11.

[69] Smith Decl. Ex. 1 at 15; Fox Decl. Ex. 3 at 15. Dr. Abdulla's reference to SSRIs generally creates additional problems of lack of fit.

[70] *Hendrix ex rel. G.P. v. Evenflo Co.*, 609 F.3d 1183, 1201 (11th Cir. 2010).

[71] *Hollander v. Sandoz Pharms. Corp.*, 289 F.3d 1193, 1210 (10th Cir. 2002).

[72] *Wade-Greaux v. Whitehall Labs., Inc.*, 874 F. Supp. 1441, 1447 (D.V.I. 1994), *aff'd*, No. 94-7199, 1994 WL 16973481 (3d Cir. Dec. 15, 1994).

[73] *DeLuca v. Merell Dow Pharms., Inc.*, 911 F.2d 941, 945 (1990).

[74] *See* Centers for Disease Control and Prevention, Congenital Heart Defects (CHD), Data and Statistics, http://www.cdc.gov/ncbddd/heartdefects/data.html (last accessed March 11, 2016).

maternal use of tobacco, alcohol, and illicit drugs.[75] Dr. Abdulla also conducted genetic tests to detect known chromosomal anomalies.[76] But the ruling-out process, by itself, cannot establish causation.[77] Because Dr. Abdulla cannot rule in Zoloft as a potential cause of the birth defects, the evidence suffers from too large an analytical gap between the data and the opinions offered.[78]

4. Dr. Kessler

Plaintiffs submit the expert report of David A. Kessler, M.D., a former Commissioner of the FDA.[79] As with Dr. Abdulla, Plaintiffs did not put forth Dr. Kessler as an expert on general causation and the Court will not allow him to offer such opinions in disregard of the course of proceedings in this MDL. Moreover, Dr. Kessler fails to create a material issue as to general causation. He states that "[w]hile I leave it to other epidemiologists to discuss the strengths and limitations of each study, none of the limitations negate the fact that the study results represent positive evidence."[80] In this litigation there is no admissible testimony from "other epidemiologists," and Dr. Kessler's own statement demonstrates that he has not conducted the analysis that the Court has explained in its earlier opinions that *Daubert* requires in this litigation.[81] Dr. Kessler's opinion that "the existence of studies that do not show a statistically

[75] Plffs.' Ex. 7 at ¶ 19.

[76] Plffs.' Ex. 7 at ¶ 15.

[77] *Cf. Hendrix*, 609 F.3d at 1202 (holding that because the expert failed to reliably rule in his theory of causation, the court did not need to "venture into the quagmire of attempting to define the parameters of a reliable process of 'ruling out' other possible causes" of the disease in question).

[78] *See General Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997) (holding that "nothing in either *Daubert* or the Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert).

[79] Robinson Decl. Ex. 24. The report is dated June 15, 2015.

[80] *Id* at ¶ 202.

[81] However, given the discussion of the epidemiological studies in the report, it appears that Dr. Kessler does recognize the importance of such evidence in establishing causation.

significant risk does not negate the statistically significant positive studies that indicate a risk," would serve to confuse a jury, particularly given that there is no evidence that Dr. Kessler himself has reconciled the contrary studies using scientifically acceptable methodology.[82] Therefore, the Court declines to consider Dr. Kessler's testimony for purposes of establishing general causation. The Court does not reach Dr. Kessler's opinions with regard to the sufficiency of the warnings on the Zoloft labels, the actions Pfizer should have taken, and the applicable regulatory issues, as these opinions cannot speak to the issue of whether Zoloft could have caused Plaintiffs' injuries.

4. *Non-Expert Evidence*

a. Case Studies and Adverse Event Reports

Plaintiffs cite reports in which doctors or patients reported adverse events that were perceived to occur after using Zoloft, including incidents of birth defects.[83] These reports are certainly relevant to the generation of study hypotheses, but are insufficient to create a material question of fact on general causation. "Although a court may rely on anecdotal evidence such as case reports, courts must consider that case reports are merely accounts of medical events. They reflect only reported data, not scientific methodology."[84] Once again, the importance of the epidemiological studies cannot be ignored: "in the face of controlled, population-based epidemiological studies which find otherwise, these case studies pale in comparison."[85] This is a

[82] Dr. Kessler's report includes two schedules entitled "Summary of Zoloft Epidemiological Study Results Concerning Birth Outcomes" (Schedule 11) and "Zoloft Epidemiological Studies – List of Strengths and Weaknesses and Cohort Summary" (Schedule 12); the report notes that all of the schedules "were prepared by staff from legal counsel at my request and subject to my review." *Id.* at 6. The Court therefore cannot conclude that these schedules represent analysis by Dr. Kessler, rather than by unknown staff employed by Plaintiffs' counsel.

[83] *See, e.g.*, Robinson Exs. 110, 152.

[84] *Rider*, 295 F.3d at 1199 (citing *Allison v. McGhan Med. Corp.*, 184 F.3d 1300, 1316 (11th Cir. 1999)).

[85] *Allison*, 184 F.3d at 1316 (citations omitted). *Accord Glastette* , 252 F.3d at 989-90 (noting that case reports do not screen out alternative causes for the adverse event and often lack analysis).

particularly salient point in the context of birth defects, which have many potential causes, known and unknown.[86]

b. Pfizer documents and foreign labels

Plaintiffs have produced a plethora of internal Pfizer documents, including discussions among Pfizer's own epidemiologists and other scientists analyzing certain epidemiological studies. The Court has ruled that statements set forth in Pfizer company documents such as literature reviews of published studies are not typical of documents that experts would generally rely upon in a causation analysis, in part because "[t]he cited studies themselves are a better source of information regarding the methods used and the results of studies of the association of interest, and it is the methods, data, and results that a statistical expert . . . is called upon to interpret."[87] The internal documents demonstrate that Pfizer employees raised questions about associations between Zoloft and birth defects and discussed possible changes to the product label, generally without reaching conclusive findings.[88] The documents may be relevant to questions of Pfizer's knowledge and actions if Zoloft were found to cause birth defects, but do not raise a genuine issue of material fact as to causation. Pfizer's epidemiologists and others reviewed the same epidemiological studies that Plaintiffs' own experts unsuccessfully attempted to use to establish causation. Neither these documents, nor draft product documents or foreign product labels containing language that advises use of birth control by a woman taking Zoloft

[86] The adverse event reports as to Zoloft are of a markedly different character from those in the *In re: Neurontin Marketing, Sales Practices, and Products Liability Litigation*, 612 F. Supp. 2d 116, 153 (D. Mass. 2009), as the reports in those cases included "dechallenge and rechallenge events," in which the adverse event stops when the patient stops taking the drug and reoccurs when the patient resumes taking the drug, as well as reports from clinical trials, which cannot be conducted with pregnant women.

[87] *In re Zoloft*, 2015 WL 7776911, at *12.

[88] *See, e.g.*, Robinson Decl. Exs. 148, 149.

constitute an admission of causation, as opposed to acknowledging a possible association.[89] In addition, as the FDA has listed Zoloft as a Category C drug, foreign labels provide at best equivocal evidence.[90]

B. Is Summary Judgment for Defendants Warranted?

The Court has carefully considered the evidence that Plaintiffs argue creates a material issue of disputed fact on causation. Without admissible expert testimony based on the epidemiological evidence, Plaintiffs instead have cobbled together evidence of biological plausibility, specific causation opinions based on an assumption that general causation has been established, and anecdotal evidence.[91] Taken together, Plaintiffs' potentially admissible evidence supports no more than an association between Zoloft and certain birth defects, and can only establish that much by ignoring the full universe of epidemiological evidence and

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[89] *See Meridia Prods. Liab. Litig. v. Abbott Labs.*, 447 F.3d 861 F.3d 861, 866 (6th Cir. 2006) (holding that a label that was the product of discussion between the FDA and the regulated party and warned that the drug "substantially increases blood pressure in some patients" constituted an admission in light of the strong language of "substantially increases" in contrast to "milder warning language such as 'is associated with.'") (capitalization omitted). This is consistent with the Court's prior rulings that establishing causation requires a "true" association:

> In general, before concluding that there is a "true" association between maternal medication use and birth defects, the teratology community requires repeated, consistent, statistically significant human epidemiological findings, and studies which address suspected confounders and biases.
>
> Epidemiological studies alone can only inform scientists that two events (*e.g.*, medication exposure and a birth defect) are associated. . . . To infer a causal relationship from an association, scientists look at well-established factors sometimes referred to as the Bradford-Hill criteria. These include: the strength of the association between the exposure and the outcome; the temporal relationship between the exposure and the outcome; the dose-response relationship; replication of findings; the biological plausibility of such an association; alternative explanations for the association; the specificity of the association (*i.e.*, does an outcome have only one cause, or several); and the consistency with other scientific knowledge.

In re Zoloft, 2015 WL 7776911, at * 3 (footnote omitted).

[90] The FDA has established five categories to indicate the potential of a drug to cause birth defects if used during pregnancy; Category C means that animal reproduction studies have shown an adverse effect on the fetus, but there are no adequate and well-controlled studies in humans, and so pregnant women should weigh the potential benefits against the potential risks. *In re Zoloft*, 26 F. Supp. 3d at 453 n.7.

[91] Plaintiffs also present excerpts from the depositions of Defendants' experts, who did not conclude that Zoloft can cause birth defects, for the uncontroverted medical fact that Zoloft crosses the placenta. *See* Robinson Decl. Exs. 36, 37.

disregarding the Court's substantive and procedural rulings on general causation. Causation must be based upon more than a possibility.

As Plaintiffs have not produced sufficient admissible evidence from which a reasonable factfinder could determine, by a preponderance of the evidence, that Zoloft could have caused Plaintiffs' injuries, the Court therefore turns to the second question implicated by Defendants' motion for summary judgment: Where does the litigation go from here?

1. Plaintiffs' Request to Delay or Deny Summary Judgment Pending Case-Specific Discovery

Plaintiffs argue that summary judgment should be denied in all cases except *Long* and *Goulet* pursuant to Federal Rule of Civil Procedure 56(d) so that all Plaintiffs have the opportunity to conduct discovery in their individual cases and to obtain differential diagnoses to support their claims.[92] However, Plaintiffs have failed to comply with the plain language of the Rule, as the argument is unsupported by affidavit or declaration. No individual plaintiff has sought to introduce his or her own expert as to general causation, and as discussed above, a differential diagnosis is insufficient to establish general causation.[93] It is also worth emphasizing, again, that the path to establishing general causation was fully laid out in pretrial orders and the Court's rulings, and the Court will not allow Plaintiffs to disregard the entire course of the MDL proceedings.[94]

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[92] The Rule provides that "[i]f a nonmovant shows by affidavit or declaration that, for specified reasons, it cannot present facts essential to justify its opposition, the court may: (1) defer considering the motion or deny it; (2) allow time to obtain affidavits or declarations or to take discovery; or (3) issue any other appropriate order." Fed. R. Civ. P. 56(d).

[93] *See Garner v. City of Ozark*, 587 F. App'x 515, 518 (11th Cir. 2014). This is not a case in which a party filed for summary judgment before expert reports were due. *See LaBarre v. Bristol-Myers Squibb Co.*, 544 F. App'x 120, 124 (3d Cir. 2013).

[94] After the Court allowed the PSC to present Dr. Jewell as an additional expert on general causation, the Court advised Plaintiffs' counsel at a general status conference that cases could be subject to a summary judgment motion even though it had not been selected as a trial case and individual discovery had not been conducted. Hr'g Tr. Feb. 23, 2015 at 26-28 [Doc. No. 1158]. Although the PSC's memorandum vaguely alludes to due process

2. Plaintiffs' Request for Dismissal without Prejudice

Plaintiffs forcefully argue that if, as the Court has determined, summary judgment is warranted, the cases should instead be dismissed without prejudice pursuant to Federal Rule of Civil Procedure 41(a)(2).[95] Dismissal under this Rule is within the sound discretion of the Court and the primary purpose in requiring court approval is to protect the other party from unfair treatment.[96] The Court considers factors such as "the defendant's effort and expense of preparation for trial, excessive delay and lack of diligence on the part of the plaintiff in prosecuting the action, insufficient explanation for the need to take a dismissal, and whether a motion for summary judgment has been filed by the defendant."[97]

This MDL has been extensively litigated for more than three years through substantial discovery from Pfizer and two rounds of *Daubert* hearings on five experts, at what must have been considerable expense. Plaintiffs did not seek Court approval to dismiss the cases without prejudice until after Defendants moved for summary judgment in the wake of the exclusion of Dr. Jewell's testimony. Plaintiffs argue that they should have the opportunity to bring the cases at a later time should the claims become viable, and that the interests of the minor Plaintiffs should be protected by preserving their right to sue in the future. The Court is not persuaded that the cases upon which Plaintiffs rely in support of these arguments augur in favor of dismissal without prejudice in this MDL.

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concerns, the argument is not developed. The Court is satisfied that all Plaintiffs had notice and opportunity to bring evidence on general causation before the Court, or to seek dismissal without prejudice of any individual cases, if they so chose.

[95] The Rule provides in relevant part that "an action may be dismissed at the plaintiff's request only by court order, on terms that the court considers proper. . . . Unless the order states otherwise, a dismissal under this paragraph (2) is without prejudice." Fed. R. Civ. P. 41(a)(2).

[96] *Grover v. Eli Lilly and Co.*, 33 F.3d 716, 718 (6th Cir. 1994) (citation omitted).

[97] *Id.*

In *In re Paoli R.R. Yard PCB Litigation*,[98] the Third Circuit held that several plaintiffs in a multi-plaintiff litigation stemming from exposure to toxic substances who asserted both property damage and personal injury claims should be permitted to dismiss without prejudice the personal injury claims because they were not presently suffering injuries, but could manifest harm from exposure in the future.[99] Significantly, the court found that there was no indication that defendants had litigated the personal injury claims, having focused on issues of causation, exposure, and non-physical injury.[100] Here, all Plaintiffs allege that the injury has occurred and the reason Plaintiffs seek to keep the litigation gates open—that they may at some point in the future be able to establish general causation—is precisely the issue that has been exhaustively litigated.

The New York district court in *In re Agent Orange Products Liability Litigation*,[101] granted dismissal without prejudice to minor plaintiffs who lacked evidence at the time to support their claims because the scientific evidence may not have been fully developed.[102] Importantly, the court concluded that the plaintiffs' attorneys had done little to advance the case while it was pending, and thus no substantial burden had been placed on the defendant.[103] Here, the issue of general causation has been thoroughly litigated, with the result that Plaintiffs cannot prevail despite having multiple opportunities to produce the required expert testimony. All of the minor Plaintiffs' lawsuits were brought by those legally authorized to pursue claims on their

[98] 916 F.2d 829 (3d Cir. 1990).

[99] *Id.*

[100] *Id.*

[101] 603 F. Supp. 239 (E.D.N.Y. 1985).

[102] *Id.* at 247.

[103] *Id.* at 248.

behalf and there is no principled basis for distinguishing the cases that happened to be selected as initial trial cases from the other cases in the MDL, as the failure to establish general causation affects all Plaintiffs equally. Dismissal without prejudice under the circumstances of this MDL and in the face of this essential defect of proof would work against the fair administration of justice. The Court recognizes that the final scientific verdict as to whether Zoloft can cause birth defects may not be delivered for many years. Nevertheless, Plaintiffs chose when to file their cases, and the Court concludes that for the Plaintiffs who have continued to pursue their claims, the litigation gates must be closed.[104]

IV. CONCLUSION

Throughout the course of this MDL, the Court's goal has been to ensure that all parties had a full and fair opportunity to develop their claims and defenses. At the end of the day, Plaintiffs have failed to raise a jury question on the necessary predicate to success in any case: that Zoloft was capable of causing their injuries. Consequently, Defendants' motion will be granted. An appropriate order will be entered.

[104] Plaintiffs do not argue that there is any basis for liability against the Wolters Kluwer Defendants in the absence of liability against Pfizer.